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(54) Title: APERTURED SHEET MATERIALS CONSISTING OF A HYDROGEL COMPOSITION

(57) Abstract: A self-supporting apertured sheet consisting essentially of a water-swellaable hydrogel composition, wherein the area of the apertures is up to about 50 % of the area of the sheet before swelling. Also provided are wound dressings comprising such sheets. Also provided is a method of making such sheets comprising the steps of: providing an apertured substrate sheet; coating an aqueous hydrogel precursor onto the apertured substrate; curing the aqueous hydrogel precursor on the substrate to form an apertured hydrogel layer on the substrate sheet; and separating the apertured hydrogel layer from the substrate sheet.

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APERTURED SHEET MATERIALS CONSISTING OF A HYDROGEL COMPOSITION

The present invention relates to apertured, water-swellaable sheet materials and to wound dressings comprising such sheet materials.

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It is known that the maintenance of a moist wound environment promotes the healing of wounds, especially burns and chronic wounds such as ulcers. However, it is also desirable to avoid excessive moisture or pooling of wound exudate on the wound, since liquid exudate causes maceration of skin adjacent to the wound and other difficulties. Furthermore, liquid exudate can leak from the wound site and contaminate clothes or bedding.

In practice, it is difficult to maintain the desired moisture level at the wound site because the rate of wound fluid production varies from wound to wound, and over time for any single wound. This can necessitate frequent dressing changes and a range of dressing types to treat different wounds.

EP-A-0123465 describes the use in surgical dressings of continuous polymer films formed from materials that have a higher moisture vapor permeability when the film is wet than when the film is dry.

EP-A-0875222 describes wound dressings comprising a non-swelling, water-impermeable apertured sheet having slits cut therein, wherein the apertured sheet is laminated to a water swellaable foam layer. Absorption of wound fluid causes the foam layer to swell, and the resulting deformation opens the slits in the apertured sheet thereby increasing the liquid permeability of the apertured sheet.

EP-A-0122085 describes wound dressings having a apertured sheet of water swellaable material laminated to a less water-swellaable layer. Slits are cut in the apertured sheet. In use, differential swelling of the apertured sheet and the underlying layer causes the slits in the apertured sheet to open, thereby increasing the permeability of the apertured sheet to wound fluid.

US-A-5352508 describes an apertured substrate web coated with a hydrogel material for use in wound dressings.

It has now been found that certain apertured, self-supporting hydrogel sheets
5 undergo swelling in water to produce water-swelled sheets having greater liquid permeability than the unswelled sheets. This is thought to be due to an increase in the average area of the apertures due to the swelling.

Accordingly, the present invention provides a self-supporting apertured sheet
10 consisting essentially of a water-swellaable hydrogel composition, wherein the apertures make up less than 50% of the area of the sheet before swelling.

Typically, the apertures make up from about 0.1% to about 50% of the area of the sheet (preferably of the wound facing area of the sheet) before swelling, more
15 typically from about 1% to about 30% of the area of the sheet before swelling, preferably from about 10% to about 25%, and more preferably from about 10% to about 20% of the area of the sheet before swelling.

The apertured hydrogel sheet enables a moist wound environment to be
20 maintained for prolonged periods, over a wide range of wound exudation rates. When the exudation rate is high, the apertured sheet expands and the resulting increase in the size of the apertures increases their liquid permeability. The sheet is thereby able to wick away wound fluid to prevent excessive moisture in the wound without removal of the hydrogel or blocking of the apertures in the
25 hydrogel. When the rate of wound exudate production falls, the hydrogel sheet shrinks and the resulting drop in liquid permeability helps to retain wound fluid at the surface of the wound. Furthermore, the hydrogel absorbs moisture vapor and functions as a humectant to preserve a moist wound contacting surface.

30 In certain embodiments, the area of the apertures is increased by at least about 25%, for example at least about 50% by swelling the sheet in water at 25°C for 60 minutes.

Typically, the sheet has from about 1 to about 30 apertures per square cm, for example from about 4 to about 15 apertures per square cm or from about 5 to about 10 apertures per square cm. In certain embodiments the apertures are
5 uniformly distributed over the surface of the sheet, preferably in a regular pattern.

The apertures are preferably small, since this results in the greatest proportional increase in liquid permeability when the hydrogel sheet swells. For example, the mean area of each aperture may be from about 0.01 to about 10 mm², preferably
10 from about 0.1 to about 4 mm², and more preferably from about 1 mm² to about 2 mm².

The apertures may have any suitable shape, as long as the size of the apertures increases when the hydrogel swells so as to increase the liquid permeability. In
15 certain embodiments, the apertures before swelling have a ratio of maximum length to maximum width of from about 1 to about 10, preferably from about 1 to about 3, and more preferably from about 1 to about 1.5. Suitable aperture shapes include round, oval or regular polygonal

20 The cross-section of the apertures may be constant (tubular) through the thickness of the hydrogel sheet. In other embodiments, the apertures may taper through the thickness of the sheet. This can result in apertures substantially in the form of truncated cones. Such apertures allow water to flow more readily in one direction through the sheet than in the opposite direction.

25

Preferably, such apertures have a base opening dimension (the maximum opening dimension in the top of the apertured sheet) of from 0.1 mm to 3 mm, and an apical opening dimension (remote from the top of the apertured sheet) of from 0.05 to 2 mm. More preferably, the apertures have a base opening dimension as
30 herein defined of from 0.5 mm to 2 mm, and an apical opening dimension of from 0.1 to 1.0 mm.

Preferably, the apertures have an average angle of taper (measured from the perpendicular to the plane of the apertured sheet) of from 10 to 60 degrees.

The apertured hydrogel sheet is self-supporting. That is to say, the apertured sheet does not have any reinforcing or supporting sheet, web, net or member embedded therein or laminated thereto. The apertured hydrogel sheet normally consists essentially of the hydrogel composition as hereinafter described. Naturally, the self-supporting nature of the sheet implies that the hydrogel composition has a minimum inherent strength. Preferably, the hydrogel composition (measured on a continuous strip (2.5 cm wide) of the hydrogel in accordance with ASTM 412) has a breaking force of 0.5- 10 N, more preferably 1- 5 N.

Preferably, the thickness of the apertured sheet (by ASTM D374-79) is from about 0.2 to about 4 mm, more preferably from about 0.4 to about 2 mm. Preferably, the hydrogel layer has a dry basis weight of from about 10 to about 1000g/m², more preferably from about 20 to about 200g/m², and most preferably from about 40 to about 100g/m².

The term "water-swellaable hydrogel composition" refers to compositions that absorb water to form a gel with water under physiological conditions of temperature and pH. Such compositions comprise medically acceptable macromolecular materials that have the ability to swell and absorb wound fluid while maintaining a strong integral structure. Normally, the hydrogel composition is substantially insoluble in water under physiological conditions, whereby the hydrogel is not washed away by the wound fluid. The hydrogel may comprise a biopolymer, i.e it may be formed from a polymer found in nature such as collagen, gelatin or alginate. The hydrogel may be bioabsorbable. That is to say, it may undergo gradual resorption *in vivo*.

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Typically, the apertured sheet according to the present invention absorbs at least about 10% w/w of water preferably at least about 25% w/w of water, more preferably at least about 50% w/w of water, and still more preferably at least about

100% w/w of water on immersion at 25°C for 60 minutes, based on the weight of the sheet before immersion.

Exemplary insoluble gels include certain cross-linked polyacrylate gels such as those described in EP-A-0676457; calcium alginate gels, cross-linked hyaluronate gels, gels of alginate derivatives such as propylene glycol alginate, and gels wherein the hydropolymer is formed from vinyl alcohols, vinyl esters, vinyl ethers and carboxy vinyl monomers, meth(acrylic) acid, acrylamide, N-vinyl pyrrolidone, acylamidopropane sulphonic acid, PLURONIC (Registered Trade Mark) (block polyethylene glycol, block polypropylene glycol) polystyrene-, maleic acid, NN-dimethylacrylamide diacetone acrylamide, acryloyl morpholine, and mixtures thereof. Suitable hydrogels are also described in US-A-5352508.

Preferably, the hydrogel composition comprises a macromolecular material selected from polyurethane gels, biopolymer gels, carboxymethyl cellulose gels, hydroxyethyl cellulose gels, hydroxy propyl methyl cellulose, polyacrylate and mixtures thereof. Suitable biopolymer gels include alginates, pectins, gelatin gels, galactomannans such as guar and xanthan, chitosan, gelatin, hyaluronates and mixtures thereof. Some of these biopolymer materials also promote wound healing.

Preferably, the gels are chemically or physically cross-linked, and the chemical cross-linking may be either covalent or ionic.

The apertured sheet may comprise at least 50% w/w based on the weight of the sheet before swelling of the gel-forming macromolecular materials, more preferably at least 75% w/w. The hydrogel material may further comprise from about 5 to about 50% by weight, preferably from 15 to 40% by weight, on the same basis of one or more humectants such as glycerol. The hydrogel material may further contain up to about 30% w/w, more preferably up to about 15% w/w on the same basis of water.

The hydrogel composition may further comprise up to about 10% w/w, preferably from 0.1% to 5% w/w of a medicament based on the weight of the composition before swelling. Suitable medicaments include antiseptics such as silver sulfadiazine, chlorhexidine, triclosan or povidone iodine, analgesics, steroids, 5 antibiotics, growth factors or mixtures thereof. Preferably, the apertured sheet according to the invention is substantially sterile.

The apertured sheet according to the present invention may in some embodiments be adhesive. In certain embodiments the hydrogel composition of the sheet itself 10 is adhesive. In other embodiments a medically acceptable pressure sensitive adhesive may be applied to a surface of the apertured sheet.

In certain embodiments, the hydrogel layer comprises a cross-linked polyacrylate hydrogel material, for example a material of the kind described in EP-A-0676457, 15 WO00/07638, or WO00/45866, the entire contents of which are incorporated herein by reference.

The present invention further provides a wound dressing comprising an apertured sheet according to the present invention.

20

Preferably, the wound dressing comprises an absorbent layer and/or a backing layer in addition to the apertured sheet, in which case the apertured sheet is preferably the wound-facing top sheet of the dressing.

25 Preferably, the dressing further comprises a backing layer over the back face of the apertured sheet. The backing layer preferably provides a barrier to passage of microorganisms through the dressing and further preferably blocks the escape of wound fluid from the dressing. The backing layer may extend beyond at least one edge of the absorbent layer to provide an adhesive-coated margin adjacent to the 30 said edge for adhering the dressing to a surface, such as to the skin of a patient adjacent to the wound being treated. An adhesive-coated margin may extend around all sides of the absorbent layer, so that the dressing is a so-called island

dressing. However, it is not necessary for there to be any adhesive-coated margin.

Preferably, the backing layer is substantially liquid-impermeable. The backing sheet is preferably semipermeable. That is to say, the backing sheet is preferably permeable to water vapour, but not permeable to liquid water or wound exudate. Preferably, the backing sheet is also microorganism-impermeable. Suitable continuous conformable backing sheets will preferably have a moisture vapor transmission rate (MVTR) of the backing sheet alone of 300 to 5000 g/m²/24hrs, preferably 500 to 2000 g/m²/24hrs at 37.5 C at 100% to 10% relative humidity difference. The backing sheet thickness is preferably in the range of 10 to 1000 micrometers, more preferably 100 to 500 micrometers.

The MVTR of the dressing according to the present invention as a whole is lower than that of the backing sheet alone, because the apertured sheet partially obstructs moisture transfer through the dressing. Preferably, the MVTR of the dressing (measured across the island portion of the dressing) is from 20% to 80% of the MVTR of the backing sheet alone, more preferably from 20% to 60% thereof, and most preferably about 40% thereof. It has been found that such moisture vapor transmission rates allow the wound under the dressing to heal under moist conditions without causing the skin surrounding the wound to macerate.

Suitable polymers for forming the backing sheet include polyurethanes and polyalkoxyalkyl acrylates and methacrylates such as those disclosed in GB-A-1280631. Preferably, the backing sheet comprises a continuous layer of a high density blocked polyurethane foam that is predominantly closed-cell. A suitable backing sheet material is the polyurethane film available under the Registered Trade Mark ESTANE 5714F.

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The adhesive (where present) layer should be moisture vapor transmitting and/or patterned to allow passage of water vapor therethrough. The adhesive layer is preferably a continuous moisture vapor transmitting, pressure-sensitive adhesive

layer of the type conventionally used for island-type wound dressings, for example, a pressure sensitive adhesive based on acrylate ester copolymers, polyvinyl ethyl ether and polyurethane as described for example in GB-A-1280631. The basis weight of the adhesive layer is preferably 20 to 250 g/m², and more preferably 50 to 150 g/m². Polyurethane-based pressure sensitive adhesives are preferred.

Preferably, the adhesive layer extends outwardly from the absorbent layer and the envelope to form an adhesive-coated margin on the backing sheet around the adhesive layer as in a conventional island dressing.

10

The area of the optional absorbent layer is typically in the range of from 1cm² to 200cm², more preferably from 4cm² to 100cm².

The optional absorbent layer may be any of the layers conventionally used for absorbing wound fluids, serum or blood in the wound healing art, including gauzes, nonwoven fabrics, superabsorbents, hydrogels and mixtures thereof. Preferably, the absorbent layer comprises a layer of absorbent foam, such as an open celled hydrophilic polyurethane foam prepared in accordance with EP-A-0541391, the entire content of which is expressly incorporated herein by reference. In other embodiments, the absorbent layer may be a nonwoven fibrous web, for example a carded web of viscose staple fibers. The basis weight of the absorbent layer may be in the range of 50-500g/m², such as 100-400g/m². The uncompressed thickness of the absorbent layer may be in the range of from 0.5mm to 10mm, such as 1mm to 4mm. The free (uncompressed) liquid absorbency measured for physiological saline may be in the range of 5 to 30 g/g at 25°

30

Preferably, the wound dressing according to the present invention is sterile and packaged in a microorganism-impermeable container.

In another aspect, the present invention provides a method of manufacture of an apertured sheet, comprising the steps of:

providing an apertured substrate sheet;

coating an aqueous hydrogel precursor onto the apertured substrate;
curing the aqueous hydrogel precursor on the substrate to form an
apertured hydrogel layer on the substrate sheet; and
separating the cross-linked hydrogel layer from the substrate sheet.

5

The substrate sheet is preferably a perforated thermoplastic film, such as a PTFE film or a polyolefin film or an ethylene vinyl acetate (EVA) film. Preferred are vacuum perforated films, such as the films with tapered apertures described in GB-A-1526778. In other embodiments the substrate sheet may be a perforated
10 metal or plastic plate, or mesh of metal or thermoplastic filaments. In certain embodiments the substrate sheet may be coated with a release coating, such as a silicone release coating, to assist peeling of the apertured sheet product from the substrate.

15 The hydrogel precursor is a pregel composition that forms an insoluble hydrogel upon cooling, polymerisation or cross-linking. Examples include aqueous sodium alginate, which can be gelled by calcium salts. Another example is guar gum, which can be gelled by borate salts. In other embodiments, the pregels are curable compositions that comprise one or more monomers and typically one or
20 more crosslinking agents and/or polymerisation initiators. Preferred monomers are acrylate esters, such as 2-hydroxyethyl methacrylate, acrylamides such as N,N-dimethylacrylamide. Also preferred are mixtures of salts or C1-C5 esters of 2-acrylamide-2-methylpropanesulfonic acid and salts or C1-C5 alkyl esters of acrylic acid (3-sulfopropyl) ester. Suitable cross linking agents are polyethylene glycol
25 diacrylates. Suitable initiators are conventional peroxide initiators.

Suitable pregel materials are the UV-curable polyacrylate pregels described for example in WO00/65143, the entire content of which is incorporated herein by reference.

30

Preferably, the viscosity of the pregel is adjusted to provide the desired thickness of the pregel layer on the substrate.

The pregel can be coated onto the substrate surface for example by spraying or slot coating or extrusion or by means of a doctor blade. Apertures may be formed in the pregel coating, for example, by applying a gas pressure differential across the coated substrate to blow apertures in the coating. Methods of this general type are described, for example, in WO93/19709. Alternatively, an apertured hydrogel coating on an apertured substrate may be made by the method described in WO00/65143, the entire content of which is incorporated herein by reference.

- 10 The apertured hydrogel sheet is preferably separated from the substrate by peeling.

In a further aspect the present invention provides a method of treatment of a wound comprising the step of applying a dressing in accordance with the present invention to the surface of the wound with the apertured hydrogel sheet contacting the wound.

Specific embodiments of the present invention will now be described further, by way of example.

20

Example 1

An apertured hydrogel sheet according to the invention is prepared as follows.

- 25 A substrate sheet is provided consisting of a polyethylene film that has been perforated with about 10 perforations per cm^2 , each perforation having a substantially conical shape as hereinbefore described, a maximum hole diameter of about 1.0 mm, an open area of 16% of the total area of the front face, a thickness by weight of about 43 micrometers and an embossed thickness of about 30 0.5 mm. Such perforated sheets are available from Tredegar Film Products, Richmond, Virginia under the Registered Trade Mark VISPORE.

The substrate sheet presents a smooth, perforated top surface. This surface is then coated with a layer of hydropolymer pregel 6 that is applied by spraying. The pregel consists of bovine gelatin in water at about 25°C. The concentration of the gelatin is adjusted in the range 5 to 20% w/w to provide the desired viscosity for a uniform, adherent layer of the desired thickness on the substrate. Suction is then applied to the back face of the substrate to vacuum perforate the pregel layer in register with the perforations in the substrate. The gelatin is then cross-linked by treatment with glutaraldehyde or formaldehyde. The cross-linked gelatin sheet is then dried at 40°C and then peeled from the substrate sheet.

10

The resulting hydrogel sheet has a dry basis weight of 100g/m² and consists of bovine gelatin cross-linked with glutaraldehyde or formaldehyde. The sheet has about 10 perforations per cm², each perforation having a maximum hole diameter in the range of about 0.8- 1.2 mm, resulting in an open area of about 5-10% of the total area of the apertured sheet. On soaking in water at 25°C for one hour the gelatin swells but does not dissolve, and it can be seen that the holes enlarge, thereby increasing the liquid permeability of the sheet.

The sheet can be packaged directly for use, or it can be made up into a multilayer wound dressing according to the invention. It can be sterilized by gamma irradiation.

In use, the dressing is removed from the package, and the apertured hydrogel sheet is applied to the wound with the hydrogel in contact with the wound to provide a sterile and absorbent dressing. The hydrogel sheet interacts in hitherto unexpected ways to provide a moist but not wet wound environment for a wide range of wounds over an extended period.

Example 2

30

An apertured sheet formed from a polyvinyl pyrrolidone (PVP) gel according to the invention is prepared from the following pregel formulation

	PVP	20%
	Water	79.16%
	Methyl paraben	0.25%
	Ethyl paraben	0.03%
5	Propyl paraben	0.05%
	Butyl paraben	0.01%
	2-phenoxyethanol	0.50%

The thus-formed gel solution is then extruded through a slot die onto a substrate
10 sheet of the same kind as in Example 1 moving at a speed of 5 m/minute, at a
coating weight of 1000 g/m². Suction is applied to perforate the pregel coating as
described in Example 1.

The pregel is then cured by passing it through a heating oven at 60 degrees. The
15 resulting cured hydrogel layer is then dried at 40°C and peeled from the substrate.

Example 3

A PTFE mold was prepared with conical projections spaced every 3mm. The
20 projections were 3mm high, and were 2mm diameter at the base and 1mm
diameter at the top of the cone. The mold was filled with a polyacrylate monomer
solution prepared as follows: 80mls of a solution made from 50% w/v 2-
acrylamido-2-methylpropane sulfonic acid; 20mls of water; 5 mls of Potassium
Chloride (5%w/v); 0.15ml of a solution prepared from 20 parts PEG400, and 6
25 parts of 1-hydroxycyclohexylphenylketone.

The monomer solution was polymerised by exposure to UV light, and the
polymerised gel was peeled from the mould, to provide a self supporting
perforated gel.

The above embodiments have been described by way of example only. Many other embodiments falling within the scope of the accompanying claims will be apparent to the skilled reader.

CLAIMS

1. A self-supporting apertured sheet consisting essentially of a water-swella-
ble hydrogel composition, wherein the area of the apertures is up to about 50% of the
5 area of the sheet before swelling.
2. An apertured sheet according to claim 1, wherein the area of the apertures
is from about 0.1% to about 50% of the area of the sheet before swelling.
- 10 3. An apertured sheet according to claim 1 or 2, having from about 1 to about
30 apertures per square cm.
4. An apertured sheet according to any preceding claim, wherein the mean
area of each aperture is from about 0.01 to about 4 mm².
- 15 5. An apertured sheet according to any preceding claim, wherein the
apertures before swelling have a ratio of length to width of from about 1 to about
10.
- 20 6. An apertured sheet of a water-swella-ble material, wherein the area of the
apertures is increased by at least 50% by swelling the sheet in water at 25°C for
60 minutes.
7. An apertured sheet according to any preceding claim, wherein the water-
25 swella-ble hydrogel composition has a tensile strength of 2-5 N in a 2.5 cm wide
strip.
8. An apertured sheet according to any preceding claim, wherein the
apertures are tapered from a front surface to a back surface of the sheet
- 30 9. An apertured sheet according to any preceding claim, wherein the sheet
absorbs at least 50% w/w of water on immersion at 25°C for 60 minutes, based on
the weight of the sheet before immersion.

10. An apertured sheet according to any preceding claim, wherein the sheet has a dry basis weight of from 10 to 1000 g/m².
- 5 11. An apertured sheet according to any preceding claim, wherein the sheet has a thickness as determined by ASTM D374-79 of from about 0.2 to about 4 mm.
12. An apertured sheet according to any preceding claim, wherein the sheet
10 material comprises a hydrogel selected from polyurethane gels, gelatin gels, pectin gels, alginate gels, glycosaminoglycan gels, hyaluronic acid gels, guar gels, xanthan gels, gels formed from starch derivatives, carboxymethyl cellulose gels, hydroxyethyl cellulose gels, hydroxypropyl methyl cellulose, polyethylene oxides and mixtures thereof.
- 15 13. An apertured sheet according to any preceding claim, wherein the hydrogel layer comprises a hydrogel selected from gels formed by polymerising or copolymerising vinyl alcohols, vinyl esters, vinyl ethers and carboxy vinyl monomers, meth(acrylic) acid, vinyl amide monomers, anionic vinyl monomers,
20 hydroxy vinyl monomers, cationic vinyl monomers containing amines or quaternary groups, ionic acrylamide derivatives, N-alkyl acrylamides, acrylate esters, ionic acrylate ester derivatives, N-vinyl pyrrolidone, acylamidopropane sulphonic acid, maleic acid, NN- dimethylacrylamide, diacetone acrylamide or acryloyl morpholine.
- 25 14. An apertured sheet according to any preceding claim, wherein the hydrogel is chemically or physically cross-linked
15. A wound dressing comprising an apertured sheet according to any preceding claim.
- 30 16. A wound dressing according to claim 15, further comprising an absorbent layer in contact with a back surface of the apertured sheet.

17. A wound dressing according to any preceding claim, wherein the absorbent layer comprises a layer of hydrophilic foam.
18. A wound dressing according to claim 15, 16 or 17, wherein the dressing further comprises a backing layer over the apertured sheet.
19. A wound dressing according to claim 18, wherein the backing layer is substantially liquid-impermeable.
20. A wound dressing according to claim 18 or 19, further comprising a layer of adhesive on the surface of the backing layer facing the apertured sheet.
21. A wound dressing according to claim 6, wherein the backing layer extends beyond at least one edge of the apertured sheet to provide an adhesive-coated margin adjacent to said edge for adhering the dressing to a surface.
22. A wound dressing according to any one of claims 16 to 21 which is sterile and packaged in a microorganism-impermeable container.
23. A method of manufacture of an apertured sheet according to any one of claims 1 to 22, comprising the steps of:
- providing an apertured substrate sheet;
 - coating an aqueous hydrogel precursor onto the apertured substrate;
 - curing the aqueous hydrogel precursor on the substrate to form an apertured hydrogel layer on the substrate sheet; and
 - separating the apertured hydrogel layer from the substrate sheet.
24. A method according to claim 23, wherein the coating of aqueous hydrogel precursor is perforated by applying a gas pressure differential across the coated substrate.

INTERNATIONAL SEARCH REPORT

International Application No

GB 02/03406

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61L15/42 A61L15/60

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61F A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 122 085 A (SMITH & NEPHEW ASS) 17 October 1984 (1984-10-17) cited in the application page 8, line 4-18 page 14, line 1-10 page 17, line 1-6 page 18 -page 19	1-24
A	GB 2 093 703 A (SMITH & NEPHEW ASS) 8 September 1982 (1982-09-08) page 1, line 59-65 page 2, line 16-30, 75-82, 93-95, 105-109	1-24
A	DE 43 08 445 A (BEIERSDORF AG) 22 September 1994 (1994-09-22) page 2, line 3-14 page 6, line 40-46	1, 23, 24
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

International Application No.

GB 02/03406

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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